

**REMARKS/ARGUMENTS**

After entry of this amendment, claims 48, 51-69, and 114-390 are pending and under consideration, claims 49-50 and 70-113 having been canceled and new claims 114-390 having been added. Claims 48, 51, 58, and 62 have been amended.

Independent claim 48 has been amended to delete "SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 69." New independent claims 131, 139, 155 are directed to SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 69, respectively. New dependent claims depending from independent claims 131, 139, 155 correspond to the claims depending from independent claim 48, *i.e.*, claims 51-57 correspond to claims 132-138, 140-146, and 156-162, respectively. Thus, new claims 131-146 and 155-162 contain no new matter.

New independent claims 114, 122, 147, 163, 171 correspond in part to claim 48. New independent claims 114, 122, 147, 163, 171, respectively, are directed to an isolated nucleic acid, comprising a sequence of nucleotides that encodes SEQ ID NOS: 58; 59; 68; 70; and 74 or a complementary sequence of any of such nucleotides have been added. Applicants note that the Examiner allowed claim 58, which is directed in part to a method of producing a recombinant beta-secretase, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 58; SEQ ID NO 59; SEQ ID NO 68; SEQ ID NO 70; and SEQ ID NO 74. New dependent claims depending from independent claims 114, 122, 147, 163, 171 correspond in part to the claims depending from independent claim 48, *i.e.*, claims 51-57 correspond to claims 115-121, 123-130, 148-154, 164-170, and 172-178, respectively. Support for new claims 114, 122, 147, 163, 171 is provided at, *e.g.*, pages 7-8 of the specification. Support for new claim 114 is also provided by original claim 50. Thus, new claims 114-130, 147-154, and 163-178 contain no new matter.

Claim 51 has been amended to improve clarity. Support of the amendment is provided at, *e.g.*, page 40, lines 27-28.

Independent claim 58 is directed to a method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 43. Claim 58 has been amended to delete "SEQ ID NO: 2;

SEQ ID NO: 56; SEQ ID NO: 57; SEQ ID NO: 58; SEQ ID NO: 59; SEQ ID NO: 60; SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 69; SEQ ID NO: 70; SEQ ID NO: 74; SEQ ID NO: 75." New independent claims 179, 185, 197, 203, 209, 215, and 221 are directed to a method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 67; SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, and SEQ ID NO: 74, respectively. New dependent claims depending from independent claims 179, 185, 197, 203, 209, 215, and 221 correspond to the claims depending from independent claim 58, *i.e.*, claims 59-63 correspond to claims 180-184, 186-190 192-196, 198-202, 204-208, 210-214, 216-220, 222-226, respectively. Thus, new claims 179-226 contain no new matter.

Independent claim 64 is directed to a heterologous cell, comprising (i) a nucleic acid molecule encoding SEQ ID NO: 43 or the complementary sequence of said nucleic acid molecule; (ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and (iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell. Claim 64 has been amended to delete "SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 69." New independent claims 279, 298, 334 are directed to SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 69, respectively. New dependent claims, which respectively depend from independent claims 279, 298, 334, correspond to the claims depending from independent claim 64, *i.e.*, claims 65-69 (as discussed below, claim 69 has been represented as new claims 227-240) correspond to claims 280-297, 299-314, and 335-353, respectively. Thus, new claims 279-314 and 335-353 contain no new matter.

Claim 69, which depends from claim 67, recites, "wherein the  $\beta$ -secretase cleavable fragment is SEQ ID NO: 82. Claim 69 has been amended to delete "SEQ ID NO: 83; SEQ ID NO: 84; SEQ ID NO: 85; SEQ ID NO: 86; SEQ ID NO: 87; SEQ ID NO: 88; SEQ ID NO: 89; SEQ ID NO: 90; SEQ ID NO: 91; SEQ ID NO: 92; SEQ ID NO: 93; SEQ ID NO: 94; SEQ ID NO: 95; and SEQ ID NO: 96." New dependent claims 227-240 are directed to  $\beta$ -secretase cleavable fragments of SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91,

SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94, SEQ ID NO: 95, and SEQ ID NO: 96 respectively.

New independent claims 241, 260, 315, 353, and 372 correspond in part to claim 64. New independent claims 241, 260, 315, 353, 372, respectively, are directed to an isolated nucleic acid, comprising a sequence of nucleotides that encodes SEQ ID NOS: 58; 59; 68; 70; and 74 or a complementary sequence of any of such nucleotides have been added. Applicants note that the Examiner allowed claim 58, which is directed in part to a method of producing a recombinant beta-secretase, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 58; SEQ ID NO 59; SEQ ID NO 68; SEQ ID NO 70; and SEQ ID NO 74. Support for new claims 241, 260, 315, 353, and 372 is provide at, *e.g.*, page 38, lines 25-28 and page 40, lines 11-16 of the specification. Thus, new claims 241, 260, 315, 353, and 372 contain no new matter. New dependent claims, which respectively depend from independent claims 241, 260, 315, 353, 372, correspond to the claims depending from independent claim 64, *i.e.*, claims 65-69 (as discussed above, claim 69 has been represented as new claims 227-240) correspond to new dependent claims 242-259, 261-278, 316-333, 354-371, 373-390.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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